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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,314	05/17/2005	David Wallach	WALLACH33	6672

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EXAMINER	
SWOPE, SHERIDAN	
ART UNIT	PAPER NUMBER
1652	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/511,314	WALLACH ET AL.	
	Examiner	Art Unit	
	Sheridan L. Swope	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *21-25 and 66-73* is/are pending in the application.

4a) Of the above claim(s) *21,22,25,68,71 and 72* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20,23,24,66,67,69,70 and 73-75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 October 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election of Invention I and sub-inventions (A) and (E), in their response of January 1, 2007, is acknowledged. The elected invention is directed to a method for treatment of rheumatoid arthritis, a disease involving IL-1, using the NIK polypeptide of SEQ ID NO: 18. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). It is acknowledged that Claims 26-34 and 42-57 have been cancelled. Claims 20-25 and 66-75 are pending. Since SEQ ID NO: 19 is an obvious over SEQ ID NO: 18, restriction between SEQ ID NO: 18 and 19 is withdrawn. Claims 21-25 and 66-75 are pending. Claims 21, 22, 25, 68, 71, and 72 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Claims 20, 23, 24, 66, 67, 69, 70, and 73-75 are hereby examined.

Priority

The priority date granted for the instant invention is October 8, 2002, the filing date of Israel 152183, which discloses the elected invention.

Oath-Objections

The Oath of May 17, 2005 is objected to for failing to recite priority to Israel 149217 or Israel 152183.

Drawings-Objections

Figures 11-15 are objected to for disclosing sequences that are not identified by a sequence identifier number (SEQ ID NO:). The sequence rules embrace all nucleotide sequences with ten or more bases and all amino acid sequences with four or more amino acids.

Said sequences must be disclosed in a sequence listing and identified by a specific SEQ ID NO: (MPEP 2421.02). 37 CFR 1.821(d) requires the use of the assigned sequence identifier number in all instances where the description or claims of a patent application discuss sequences, regardless of whether a given sequence is also embedded in the text of the description or claims of an application. Applicant is required to check the disclosure completely and to make corrections to identify all of the sequences disclosed therein by sequence identifier numbers.

Figures 4-8 and 10 are objected to because each Y-axis is not labeled.

Abstract-Objection

The Abstract is objected to for having an undefined abbreviation.

Specification-Objections

The first paragraph of the specification should be amended to recite the status of parent applications.

The specification is objected to because the table on page 57 is not numbered.

Claims-Objections

The claim set is objected to for not beginning with a sentence of which the claims are an object e.g., "We claim" or "The claims are".

Claims 20, 23, 24, 66, 67,69, 70, and 73-75 are objected to for having an abbreviation, NIK, that is not defined.

Claims 74 and 75 are object to for reciting non-elected subject matter.

To improve the grammar of Claim 20, it is suggested that the phrase "involving signaling of a cytokine through IL-2 cγc in the pathogenesis of said disease" be set off by commas.

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 20, 23, 24, 66, 67, 69, 70, and 73-75 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the following reasons.

For Claims 20, the phrase "therapeutically effective" renders the claim indefinite. It is unclear what parameters of the disease are to be analyzed and how effective the treatment must be in order to be "therapeutically effective". For Claim 20, the phrase "functional derivative" also renders the claim indefinite. It is unclear what function(s) said derivative has. The skilled artisan would not know the metes and bound of the invention. Claims 23 and 24, as dependent from Claim 20, are indefinite for the same reason.

For Claim 66, the phrases "therapeutically effective" and "functional derivative" render the claim indefinite for the reasons stated for Claim 20 above. Claim 67, as dependent from Claim 66, is indefinite for the same reason.

For Claims 69, 70, and 73, the phrases "therapeutically effective" and "functional derivative" render the claims indefinite for the reasons stated for Claim 20 above. For Claims 69, 70, and 73, the phrase "a host" also renders the claims indefinite. It is unclear whether "a host" is meant to mean "a patient", "a subject", "a cell" or some other organism to be treated. Claims 74 and 75, as dependent from Claims 73 and 69, respectively, are indefinite for the same reasons.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claims 20, 23, 24, 66, 67, 69, 70, and 73-75 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating allograft rejection and adult T-cell leukemia using the polypeptide of SEQ ID NO: 19 (see rejection under 35 U.S.C. 103), does not reasonably provide enablement for treating any disease involving signaling via any IL-2 cγc using any variant of any NIK. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In regards to this enablement rejection, the application disclosure and claims are compared per the factors indicated in the decision In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). These factors are considered when determining whether there is sufficient evidence to support a description that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. The factors include but are not limited to: (1) the nature of the invention; (2) the breath of the claims; (3) the predictability or unpredictability of the art; (4) the amount of direction or guidance presented; (5) the presence or absence of working examples; (6) the quantity of experimentation necessary; (7) the relative skill of those skilled in the art. Each factor is here addressed on the basis of a comparison of the disclosure, the claims, and the state of the prior art in the assessment of undue experimentation.

Claims 20, 66, 67, 69, 70, and 73-75 are so broad as to encompass treatment of any disease involving signaling via any IL-2 cγc using any variant of any NIK. Claims 23 and 24 are so broad as to encompass treatment of any disease involving signaling via any IL-2 cγc using the polypeptide of SEQ ID NO: 19 or 18, respectively. The scope of these claims is not commensurate with the enablement provided by the disclosure with regard to the large number of diseases to be treated with a large number of polypeptides.

The specific reagents and steps used for treating any disease determine the method's success. Predictability of which steps and reagents can be used to obtain treatment requires a knowledge of, and guidance with regard to how said steps and reagents relate to the desired disease and treatment thereof. In addition, predictability of which of the large number of diseases can be treated with NIH, or any variant thereof, requires a knowledge of, and guidance with regard to the molecular basis of each disease and how the molecular basis relates to the function of NIK. However, in this case the disclosure fails to teach how to treat any disease using any NIK, or variant thereof; it is the art that teaches treating allograft rejection and adult T-cell leukemia using the polypeptide of SEQ ID NO: 19.

While methods for testing the ability of a polypeptide to treat some diseases are known, it is not routine in the art to screen an essentially unlimited number of polypeptides in multiple treatment assays, as encompassed by the instant claims. Furthermore, the steps and reagents to be used with a reasonable expectation of success in obtaining the desired treatment of any IL-2 cγc mediated disease are limited and may be unpredictable (O'Shea et al, 2002), as acknowledged by Applicants (specification; pg 7, parg 4). In addition, one skilled in the art

would expect any tolerance to modification of a method for treating a given disease to diminish with each further and additional modification of steps and reagents used.

The specification does not support the broad scope of Claims 20, 66, 67, 69, 70, and 73-75, which encompass treatment of any disease involving signaling via any IL-2 cγc using any variant of any NIK. The specification does not support the broad scope of Claims 23 and 24, which encompass treatment of any disease involving signaling via any IL-2 cγc using the polypeptide of SEQ ID NO: 19 or 18, respectively. The specification does not support the broad scope of Claims 20, 23, 24, 66, 67, 69, 70, and 73-75 because the specification does not establish: (A) which diseases, involving signaling via any IL-2 cγc, can be treated with any NIK; (B) which NIK variants can be used to treat any disease involving signaling via any IL-2 cγc (C) the general tolerance of treatment to modification of any NIK and extent of such tolerance; (D) a rational and predictable scheme for treating any disease using any NIK variant; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices of NIK variants is likely to be successful in treating a large number of diseases involving signaling via any IL-2 cγc.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including treating any disease involving signaling via any IL-2 cγc using any variant of any NIK. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the identity of the NIK variants to be used as well as the identity of diseases to be successfully treated is unpredictable and the experimentation left to those skilled in the art is

unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Written Description

Claims 20, 23, 24, 66, 67, 69, 70, and 73-75 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

These claims are directed to a genus of methods for treating any disease involving signaling via any IL-2 cγc using any variant of any NIK. The specification teaches no such methods. Moreover, the specification fails to describe any representative species of the genus by any identifying characteristics or properties other than the functionality of being a method for treating any disease involving signaling via any IL-2 cγc using any variant of any NIK. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 20 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tinubu et al, 1994 in view of Yamada et al, 2000 and further in view of Luftig et al, 2001. Tinubu et al teach treating allograft rejection by administering an antibody that blocks IL-2 binding to its receptor (Table II). Tinubu et al do not teach treating allograft rejection by administering NIK or a variant thereof. Yamada et al teach that NIK is required for IL-2 production (Table II) and regulates allogenic skin graft rejection (Table III). Luftig et al teach a dominant negative variant of NIK (DN-NIK) consisting of residues 624-947 (Fig 1), which is the same as SEQ ID NO: 19 herein. It would have been obvious to a person of ordinary skill in the art to administer the DN-NIK of Luftig et al to block NIK-mediate production of IL-2 in order treat allograft rejection. Motivation to do so derives from the desire to prolong allograft transplants. The expectation of success is high, as both NIK and IL-2 are linked to allograft rejection and IL-2 production is mediated by NIK. Therefore, Claims 20 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tinubu et al, 1994 in view of Yamada et al, 2000 and further in view of Luftig et al, 2001.

Claims 20 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Waldmann et al, 1993 in view of Yamada et al, 2000 and further in view of Luftig et al, 2001. Waldmann et al teach treating adult T-cell leukemia by administering an antibody that blocks IL-2 binding to its receptor (Table 2). Waldmann et al do not teach treating adult T-cell leukemia by administering NIK or a variant thereof. The teachings of Yamada et al and Luftig et al are described above. It would have been obvious to a person of ordinary skill in the art to administer the DN-NIK of Luftig et al to block NIK-mediate production of IL-2 in order treat adult T-cell leukemia. Motivation to do so derives from the desire to prolong the life and well-being of

patients having adult T-cell leukemia. The expectation of success is high, as IL-2 promotes adult T-cell leukemia and IL-2 production is mediated by NIK. Therefore, Claims 20 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Waldmann et al, 1993 in view of Yamada et al, 2000 and further in view of Luftig et al, 2001.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Art Unit 1652